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In multicellular organisms, cellcell junctions are involved in all aspects of tissue morphogenesis, including regulation of cell shape and movement. To establish junctions, cytoplasmic proteins that interact with the actin cytoskeleton must stabilize adhesion molecules. For example, catenins connect cadherins to the cytoskeleton and mutations in catenin proteins significantly impact morphogenesis. A previously isolated hypomorphic allele of the *C. elegans* α-catenin homolog, *hmp-1(fe4)*, exhibits 70 lethality and body shape defects (Pettitt et al., 2003, JCB 162, 1522). In continuing efforts to identify regulators of the cadherincatenin complex, we conducted a genome-wide RNAi screen to identify genes whose loss of function enhances the *hmp-1(fe4)* phenotype. We uncovered MAGI-1, a vertebrate tight junction protein known to interact with actin-binding proteins (Patrie et al., 2002, JBC 277, 3018390). We have shown that *C. elegans* MAGI-1 genetically interacts with *hmp-1*/α-catenin and *hmp-2*/β-catenin, suggesting that MAGI-1 may modulate cadherincatenin function during morphogenesis. MAGI-1 localizes at the *C. elegans* apical junction, but is surprisingly basal to the cadherincatenin complex. In addition, MAGI-1 junction localization is not dependent on β-catenin, in contrast to what has been shown in tissue culture (Dobrosotskaya et al., 2000, BBRC 270, 90309). We are currently examining whether MAGI-1 modulates actin dynamics at junctions and we are trying to identify and characterize proteins that interact with MAGI-1 to further assess how MAGI-1 functions in a living organism.

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Program/Abstract # 226
Inhibition of Nodal signaling affects epiblast cell movement in the pre-streak chick blastoderm
Nariaki Yanagawa, Toshiyuki Yamagishi, Yuji Nakajima
Department of Anatomy and Cell Biology, Osaka City University Graduate School of Medicine, Osaka, Japan

Before the onset of gastrulation in the chick blastoderm, lateral epiblast cells move to posterior mid-line of the epiblast coincident with an anterior movement of the posterior epiblast. This cellular movement that occurs in the epithelial-epiblast was described as Polonaise movement (Graper, 1929), however cellular and molecular mechanisms regulating the Polonaise movement remain uncertain. Using explants and whole embryo culture models of chick blastoderm, we investigated the signaling regulating the Polonaise movement before the formation of the primitive streak. In situ hybridization showed that Nodal was expressed in the posterior epiblast and FGF8 in the developing hypoblast at early blastula stages. In cultured explants that were obtained from the posterior blastoderm, either Lefty1, SB431542 (ALK4 antagonist) or siRNA to Nodal inhibited the initial migration of explants at 10 and 20h in culture, during which explants developed to late blastula and early gastrula, respectively. Perturbation of Nodal signaling also affected a movement of DiI marked epiblast cells in cultured blastoderm. Cultured blastoderm treated with Nodal antagonist failed to form primitive streak as well as expression of Brachyury. Inhibition of FGF signaling did not affect the initial migration of the cultured explants but affected after 30 to 40h in culture. Results suggest that Nodal signaling may play an important role in cellular movement (Polonaise movement) that occurs in the epithelial-epiblast of the pre-streak blastoderm.

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Program/Abstract # 227
Early embryonic cell movement regulated by the availability of cholesterol
Sara C. Ahlgren[a,b], Evyn Loucks[a], Diana Snyder[a], Tyler Schwend[a,c]
[a]*Program in Dev. Bio., Children's Mem. Res. Center, Chicago, IL, USA*
[b]*Department of Ped., Northwestern Univ. Feinberg Sch. Med., Chicago, IL, USA*
[c]*Int. Grad. Program, Northwestern Univ. Feinberg Sch. Med., Chicago, IL, USA*

Embryonic cell movement is essential for morphogenesis and the establishment of body shapes. Zebrafish embryos undergo a process termed epiboly in which cells move from the animal pole to envelop the yolk. We have cloned the cholesterol trafficking protein, npc1, from the zebrafish embryo. At early cleavage stages, npc1 is found ubiquitously in all blastomeres, before becoming restricted to the yolk syncytial layer during epiboly. Later, npc1 is widely expressed in the developing brain, as with mammalian Npc1. Mutations in NPC1 lead to the disease NiemannPick type C in humans. In order to disrupt npc1 we developed 2 anti-sense morpholinos (MOs) targeted to either the start site or a splice site within npc1. Injection of MOs into the 12 cell zebrafish embryo resulted in a dose-dependent delay in epiboly. This delay is accompanied by the accumulation of cholesterol within cells, suggesting that inhibition of zebrafish npc1 results in abnormal cholesterol trafficking. Zebrafish injected with npc1 MO display a disorganized actin cytoskeleton and the actin ring on the leading edge of epiboly is missing. There are additional defects in convergence and extension movements, although anteriorposterior patterning occurs normally. Cells with accumulated cholesterol also appear to be morphologically blebbing, suggesting that they are undergoing apoptosis. The data presented here extends our understanding about the role of cholesterol during cell movements in early development.

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Program/Abstract # 228
The ascidian mouth develops from the anterior neuropore: Implications for chordate evolution
Michael T. Veeman, Erin Newman-Smith, El-Nachef Danny, Smith C. Smith
Department of Molecular, Cell and Developmental Biology, USA

The ascidian oral siphon is homologous by both molecular and functional criteria to the vertebrate mouth. It develops from a larval oral siphon primordium (OSP) in the form of a dorsal placode-like invagination just anterior to the larval neural tube. A so-called neurohypophyseal duct (ND) has been shown to connect the OSP with the lumen of the neural tube at late larval stages, but the OSP was thought to form independently of the neural tube with the ND forming later. Here we use a stable Etr1GFP transgene and probes for nuclei and actin to image neural tube closure in fixed and live *Ciona savignyi*. In contrast with the previous model, we find that the OSP maintains topological continuity with the neural tube from its beginning, with a connection to the gut endoderm forming considerably later. We show that although a placode-like intermediate stage is present, the OSP develops from the anterior neuropore. Despite this unexpected role for the neuropore in *Ciona*, there are striking similarities between mouth formation in ascidians and vertebrates, with the stomodeum forming between an anterior, adhesive, columnar mucosecretory organ (i.e., the adhesive palps in *Ciona* and the cement gland in *Xenopus*) and the hollow, dorsal neural tube. These results suggest a new model in which the tubular topology of the chordate CNS is derived from its coevolution with a preexisting deuterostome mouth.

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Program/Abstract # 229
Conserved and divergent mechanisms of patterning and regeneration in vertebrate appendages
Randall Dahn
The Mount Desert Island Biological Laboratory, Salisbury Cove, Maine, USA